

Neuromodulatory Subcortical Systems And Sleep In Alzheimer’s Disease: A Review Of Therapeutic Interventions

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Key Takeaway: The basal forebrain (an NSS region linked to sleep) is among the earliest sites of neurodegeneration in AD. Therapies like melatonin/CBT (circadian regulation, N=6) and Z-drugs, trazodone, light therapy (improved sleep quality, N=12) reduce sleep disturbances in AD via NSS effects.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Alzheimer’s disease (AD) continues to evade many emerging potential treatment options. This has led to the exploration of more areas including its intersection with sleep and the Neuromodulatory subcortical systems(NSS).This study aims to shed light on therapeutic interventions at the intersection between NSS, sleep and AD	A search was conducted across three electronic databases- PubMed, MEDLINE, and Web of Science to identify studies published up to February 19th, 2025. Only peer-reviewed studies published in English were included. RCTs, meta-analysis, and reviews were included if they related to the therapeutic interventions for AD at the intersection of NSS and Sleep. Newspaper articles, editorials, and studies not related to the topic were excluded. The studies were screened using the Rayyan software.	133 articles were received from the screening and 36 papers met the inclusion criteria upon full text screening. It was revealed across studies that the basal forebrain, a neuromodulatory centre, involved with sleep, is among the first regions of the brain to experience neurodegeneration in AD. Melatonin and Cognitive Behavioral Therapy, by regulating the circadian rhythm (N=6), Z-drugs (Zolpidem and Zopiclone), Trazidone and light therapy, by improving sleep quality and decreasing nocturnal awakenings (N=12), reduced sleep disturbances in AD by acting on the NSS. 12 ●Melatonin & Cognitive Behavioural Therapy Regulating the Circadian Rhythm 6 ●Z-drugs, Trazidone & Light Therapy Improving Sleep Quality & Decreasing nocturnal awakesness Fig 1: NSS Therapies and respective Effects	studies have shown that these sleep therapies offer potential in improving the quality of life of patients with AD. However, there is a need to conduct more studies to ascertain their me mechanisms of action and effectiveness in slowing down the progression of AD.	1. Hajjo R, Sabbah DA, Abusara OH, Al Bawab AQ. A review of the recent advances in Alzheimer’s disease research and the utilization of network biology approaches for prioritizing diagnostics and therapeutics. <i>Diagnostics</i> (Basel). 2022;12(12):2975. 2. Soria Lopez JA, González HM, Léger GC. Alzheimer’s disease. <i>Handb Clin Neurol</i>. 2019;167:231-255. doi: 10.1016/B978-0-12-804766-8.00013-3. 3. Wang C, Holtzman DM. Bidirectional relationship between sleep and Alzheimer’s disease: role of amyloid, tau, and other factors. <i>Neuropsychopharmacology</i>. 2020 Jan;45(1):104-120. doi: 10.1038/s41386-019-0478-5. Epub 2019 Aug 13.
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